Clean Version of Entire Pending Claim Set:
as of the January 22, 2001 Amendment

1. A preparation for the transport of at least one active agent through the skin or mucous membrane of a mammal, comprising transfersomes suspended in a pharmaceutically acceptable medium for application onto the skin or mucous membrane of a mammal, said transfersomes comprising liquid droplets encompassed within a sheath comprising at least two amphiphilic lipid components which differ in their solubility in said pharmaceutically acceptable medium by a factor of at least 10, said two amphiphilic compounds being selected such that said transfersomes are capable of undergoing sufficient deformation to pass through said skin or mucous membrane without being solubilized.

3. The preparation of claim 1 , wherein the solubility of the more soluble component(s) is at least 10^{-3} to 10^{-6} M and the solubility of the less soluble component(s) isat least 10^{-6} to 10^{-10} M.

4. The preparation of claim 1, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between 10 and 10^{7}.

5. The preparation of claim 1, wherein the preparation through said skin or mucous membrane at least 0.001% of the permeability of small molecules, which permeate essentially without being impeded.

6. The preparation of claim 1, wherein the permeation capability relative to reference particles $P_{(transfer.)}/P_{(refer.)}$, the reference particles being water is between 10^{-5} and 1.

7. The preparation of claim 1, wherein said transfersomes contain an active agent in said liquid droplet, in said sheath, or in both said liquid droplet and said sheath .

8. The preparation of claim 1, wherein the vesicle radius of the transfersome is between about 25 nm and about 500 nm.

9. The preparation of claim 7, wherein the sheath is a double layer.

10. The preparation of claim 1 , wherein said amphiphilic components comprise lipids of different polarity.

11. The preparation of 1 , wherein at least one amphiphilic lipid component is selected from the group consisting of a diacyl or a dialkyl glycerophosphoethanolamino azo polyoxyethylene derivative, a didecanoyl phosphatidyl choline, a diacyl phosphooligomaltobionamide, a glyceride, a glycerophospholipid, a isoprenoid lipid, a sphingolipid, a steroid, a sterol, a sulfur-containing or a hydrocarbon-containing lipid or a different lipid, which forms stable structures, such as double layers, a half protonated liquid fatty acid, a phosphatidyl choline, a phosphatidyl ethanolamine, a phosphatidyl

glycerol, a phosphatidyl inosital, a phosphatid acid, a phosphatidyl serine, a sphingomylein or a sphingophospholipid, glycosphingolipid, a cerebroside, a ceramide polyhexoside, a sulfatide, a sphingoplasmalogen a ganglioside or other glycolipid, or a synthetic lipid, a dioleoyl, a dilinolyl, a dilinolenyl, a dilinoloyl, a dilinolinoyl or a diarachinoyl, a dilauroyl, a dimyristoyl, a dilalmitoyl, a distearoyl phospholipid or a corresponding dialkyl or a sphingosin derivative, a glycolipid or other identical chain or a mixed chain acyl lipid and an alkyl lipid.

12. The preparation of claim 1 wherein the less soluble amphiphilic lipid component is selected from the group consisting of a myristoleoyl, a palmitoleoyl, a petroselinyl, a petroselaidyl, a oleoyl, elaidyl, a cis- or trans- vaccenoyl, a linolyl, a linolenyl, a linolaidyl, a octadecatetraenoyl, a gondoyl, a eicosaenoyl, a eicosadienoyl, a eicosatrienoyl, a arachidoyl, a cis- or trans-docosaenoyl, a docosadienoyl, a docosatrienoyl, a docosatetraenoyl, a caproyl, a lauroyl, a tridecanoyl, a myristoyl, a pentadecanoyl, a palmitoyl, a heptadecanoyl, a stearoyl or a nonadecanoyl, a glycero-phospholipid or a corresponding chain-branched derivative or a corresponding sphingosin derivative, a glycolipid or an acyl lipid or a alkyl lipid; and the more soluble component or components derived from one of the less soluble components derivatized with a butanoyl, a pentanoyl, a hexanoyl, a heptanoyl, a octanoyl, a nonanoyl, a decanoyl, a dodecane, a undecanoyl, a monosaturated substituent thereof, a polyunsaturated substituent thereof and a chain-branched substituent thereof.

13. The preparation of claim 1, wherein the total content of the amphiphilic components is between 0.01 and 40 % by weight of the preparation.

15. The preparation of claim 1, wherein the active ingredient is selected from the group consisting of an adrenocorticostatic agent, a β-adrenolytic agent, an androgen or antiandrogen, an anti-parasitic, an anabolic, an anesthetic or an analgesic, an analeptic, an anti-allergic, an anti-arrhythmic, an anti-arteriosclerosis, an anti-asthmatic or a bronchospasmolytic agent, an antibiotic, an anti-depressive or an anti-psychotic agent, an anti-diabetic agent, an antidote, an anti-emetic, an anti-epileptic, an anti-fibrinolytic, an anti-convulsive or an anti-cholinergic agent, an enzyme, a coenzyme, a corresponding coenzyme inhibitor, an antihistamine, an antihypertensive drug, a biological activity inhibitor, an antihypotensive agent, an anticoagulant, an anti-mycotic, an antimyasthenic agent, an active ingredient against Parkinson's or Alzheimer's disease, an anti-phlogistic, a anti-pyretic or an anti-rheumatic agent, an antiseptic, a respiratory analeptic or a stimulating agent, a broncholytic, a cardiotonic or a chemotherapeutic agent, a coronary dilator, a cytostatic agent, a diuretic, a ganglion blocker, a glucorcorticoid, a therapeutic agent for influenza, a hemostatic agent, a hyptonic agent, an immunoglobulin or a fragment or a different immunological or a receptor substance, a bioactive carbohydrate, a bioactive carbohydrate derivative, a contraceptive, a migraine agent, a mineral corticoid, a morphine antagonist, a muscle relaxant, a narcotic, a neural therapeutic agent or a CNS therapeutic agent, a nucleotide or a polynucleotide, a neuroleptic agent, a neuron transmitter, a neuron transmitter antagonist, a peptide, a peptide derivative , an ophthalmic agent, a para-sympathicomimetic or para-sympathicolytic agent, a protein, a

protein derivative, a psoriasis/neurodermatitis agent, a mydriatic agent, a mood elevator, a rhinological agent, a sleeping draft or a sleeping draft antagonist, a sedative, a spasmolytic, a tuberculosis agent or a urological agent, a vasoconstrictor or a vasodilator, a virostatic agent or a wound-healing agent, diclofenac and ibuprofen.

16. The preparation of claim 1, wherein the active ingredient is a nonsteroidal anti-inflammatory drug selected from the group consisting of diclofenac, ibuprofen, and a lithium, sodium, potassium, cesium, rubidium, ammonium, monoethyl, dimethyl, trimethylammonium or ethylammonium salt thereof.

17. The preparation of claim 10, wherein the less polar amphiphilic lipid component is a phospholipid, and a second, more soluble amphiphilic component is an active ingredient the concentration of the more soluble component(s) being between 0.01% by weight and 15% by weight.

18. The preparation of claim 1, wherein the preparation comprises consistency modifiers selected from the group consisting of a hydrogel, an antioxidant selected from the group consisting of a probucol, a tocopherol, a BHT, an ascorbic acid, a desferroxamine or a stabilizer selected from the group consisting of a phenol, a cresol, and a benzyl alcohol.

19. The preparation of 1 , wherein the active ingredient is a growth regulating substance.

20. The preparation of claim 1, wherein the active ingredient is selected from the group consisting of an insecticide, a pesticide, a herbicide or a fungicide.

21. The preparation of claim 1 , wherein the active ingredient is an allurement.

22. A method for producing a preparation for transporting at least one active ingredient through the skin or mucous membrane of a mammal, comprising:

a selecting at least two amphiphilic lipid components which differ in their solubility in a pharmaceutically acceptable medium by a factor of at least 10;

b. suspending transfersomes containing said at least two amphiphilic lipid components in said pharmaceutically acceptable medium for application onto the skin or mucous membrane, said transfersomes comprising liquid droplets encompassed within a sheath comprising said at least two amphiphilic lipid components, said amphiphilic lipid components being selected such that said transfersomes are capable of undergoing sufficient deformation to pass through said skin or mucous membrane without being solubilized;

c. including one or more solubilizing components to provide adequate deformability to said transfersomes to pass through said skin or mucous membrane without being solubilized, if necesssary, such that the content of solubilizing components is less than 0.1 mole percent, based on the content of said amphiphilic lipid components, at which the

solubilizing point of the enveloped droplets is reached; and

d. adjusting the content of amphiphilic lipid components such that the ability of the transfersomes to permeate through said skin or mucous membrane is from about 0.001% to about 0.1% of the permeability of water.

23. The method of claim 22, wherein the content of said amphiphilic components are adjusted, so that the permeation relative to water is between 10^{-5} and 1.

24. The method of claim 22 wherein the permeation capability is determined by filtration, under pressure, through a fine-pored filter or by controlled mechanical whirling up, shearing or comminuting.

25. The method of claim 22, wherein said transfersomes are produced by a method selected from the group consisting of filtration, treatment with ultrasound, stirring, shaking and other mechanical comminuting effects.

26. The method of claim 22 preparation is produced from at least two amphiphilic components of different polarity, at least one polar liquid and at least one active ingredient.

27. The method of claim 22, wherein said amphiphilic component(s) comprises or contains the active ingredient, and said transfersomes are formed from at least two amphiphilic components of different polarity and at least one polar liquid.

28. The method of claim 22 wherein said amphiphilic components and a hydrophilic substance are mixed separately with an active ingredient and optionally brought into solution,and then combined to form transfersomes.

29. The method of claim 22 wherein said amphiphilic components, either as such or dissolved in a physiologically compatible solvent or a dissolving intermediary, which is miscible with a polar liquid or liquids, are combined with a polar solution.

30. The method of claim 22, wherein said transfersomes are formed by a method selected from the group consisting of stirring; evaporation from a reverse phase; an injection method; a dialysis method; electrical stressing; thermal stressing; a mechanical stressing selected from the group consisting of shaking, stirring, homogenizing, ultrasonicating, rubbing, freezing, thawing, heating, and cooling; high pressure filtration; and low pressure filtration.

31. The method of claim 22 , wherein the formation of the transfersomes is brought about by filtration and the filter material used in said filtration has a pore size of 0.01 μm to 0.8 μm.

32. The method of claim 22 further comprising including an active ingredient in said transfersomes, and forming said transfersomes such that the association between said transfersomes and said active ingredient takes place at least partially after transfersome formation.

33. The method of claim 22 wherein shortly before use, the are prepared from a concentrate or lyophilisate.

34. The preparation of claim 4, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between 10^2 and 10^6.

35. The preparation of claim 4, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between 10^3 and 10^5.

36. (New) The preparation of claim 6, wherein the permeation capability relative to reference particles $P_{(transfer.)}/P_{(refer.)}$, the reference particles being water is between 10^{-4} and 1.

37. The preparation of claim 6, wherein the permeation capability relative to reference particles $P_{(transfer.)}/P_{(refer.)}$, the reference particles being water is between 10^{-2} and 1.

38. The preparation of claim 8, wherein the vesicle radius is between about 50 nm and about 200 nm.

39. The preparation of claim 8, wherein the vecicle radius is between about 80 nm and about 100 nm.

40. The preparation of claim 13, wherein the total content of the amphiphilic components is between about 0.1 and 15% by weight.

41. The preparation of claim 13, wherein the total content of the amphiphilic components is between about 1 and 10% by weight.

42. The preparation of claim 17, wherein the concentration of the more soluble component(s) is between 0.1% by weight and 10% by weight.

43. The preparation of claim 17, wherein the concentration of the more soluble component(s) is between about 0.5% by weight and 3% by weight.

44. The preparation of claim 17, wherein the total lipid concentration being between about 0.5% by weight and 15% by weight.

45. The preparation of claim 17, wherein the total lipid concentration being between about 1% by weight and 10% by weight.

46. The preparation of claim 1, further comprising one or more solubilizing components in an amount effective to provide adequate deformability to said transfersomes, such that said transfersomes are capable of passing through said skin or mucous membrane without being solubilized, the amount of solubilizing components included in said preparation being less than 0.1 mole percent at which the solubilizing point of the enveloped droplets is reached, based on the content of said amphiphilic lipid components.

47. The preparation of claim 1, further comprising an active ingredient contained in said sheath.

48. The preparation of claim 1, further comprising an active ingredient contained in said liquid droplets.

49. The method of claim 23, wherein the permeation relative to reference particles, is between 10^{-4} and 1.

50. The method of claim 23, wherein the permeation relative to reference particles, is between 10^{-2} and 1.

51. The method of claim 31, wherein the filter material has a pore size of 0.05 to 0.3 μm.

52. The method of claim 31, wherein the formation of the filter material has a pore size of 0.08 to 0.15 μm.